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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/349,194	07/07/99	BUECHLER K	244/121

HM12/1004

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EXAMINER	
GABEL, G	
ART UNIT	**PAPER NUMBER**
1641	9

DATE MAILED: 10/04/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trad marks

Office Action Summary

Application No.	Applicant(s)
09/349,194	Buechler et al.
Examiner	**Group Art Unit**
Gailene R. Gabel	1641

☒ Responsive to communication(s) filed on *Jul 11, 2000*

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) *1 and 55-133* is/are pending in the applicat

Of the above, claim(s) _____ is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *85-96, 102-106, and 114-133* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☒ Claims *1 and 55-133* are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☒ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachm nt(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *3*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

— SEE OFFICE ACTION ON THE FOLLOWING PAGES —

DETAILED ACTION

Election/Restriction

1. Applicants' preliminary amendment and election of Group III, claims 85-96, 102-106, and 114-133, with traverse, in Paper Nos. 2 and 8 are acknowledged and have been entered. Claims 2-54 have been canceled. Claims 55-133 have been added. Claims 1 and 55-133 are pending. Accordingly, claims 85-96, 102-106, and 114-133 are under examination.

Applicant's traversal of the restriction requirement in Paper No. 8 is acknowledged. The traversal is on the grounds that no serious burden is imposed into the Examiner due to the identical nature of the claimed inventions.

This is not found persuasive because restriction requirements are set forth for reasons of patentable distinction between each independent invention so as to warrant separate classification and search. The record set forth in the previous restriction requirement clearly indicated that the delineated inventions are in fact patentably distinct each from the other or independent from the other. The requirement is still deemed proper and is therefore made FINAL for reasons of record.

Oath/Declaration

2. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:

It does not identify the post office address of each inventor. A post office address is an address at which an inventor customarily receives his or her mail and may be either a home or business address. The post office address should include the ZIP Code designation.

Specification

3. Applicant is reminded of the proper language and format for an abstract of the disclosure.

The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 250 words. It is important that the abstract not exceed 250 words in length since the space provided for the abstract on the computer tape used by the printer is limited. The form and legal phraseology often used in patent claims, such as "means" and "said," should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

The language should be clear and concise and should not repeat information given in the title. It should avoid using phrases which can be implied, such as, "The disclosure concerns," "The disclosure defined by this invention," "The disclosure describes," etc.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 85-96, 102-106, and 114-133 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Regarding claim 85, "and/or" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d). See also claim 88, 91, 94, and 119.

Claim 85 is indefinite and incomplete for omitting essential elements, such omission amounting to a gap between the steps. See MPEP § 2172.01. In this case, it is unclear how signal production is effected by an antibody in the absence of a label. See also claims 88, 91, 94, 102, 114, 119, 124, and 129.

Claim 86 and 87 have improper antecedent basis problems in reciting "An assay according to claim 85". Change to --The assay according to claim 85-- for proper antecedent basis.

Claim 89 and 90 have improper antecedent basis problems in reciting "An assay according to claim 88". Change to --The assay according to claim 88-- for proper antecedent basis.

Claim 92 and 93 have improper antecedent basis problems in reciting "An assay according to claim 91". Change to --The assay according to claim 91-- for proper antecedent basis.

Claim 95 and 96 have improper antecedent basis problems in reciting "An assay according to claim 94". Change to --The assay according to claim 94-- for proper antecedent basis.

Claim 102 is vague and indefinite in reciting "any (cardiac specific isoform...)" because it is unclear what is encompassed by the term "any" as used in the claim.

The phrase "approximately equal" in claim 104 is a relative term which renders the claim indefinite. The phrase "approximately equal" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. See also claims 116, 121, 126, and 131.

Claim 103 - 106 have improper antecedent basis problems in reciting "An assay according to claim 102". Change to --The assay according to claim 102-- for proper antecedent basis.

Claim 115-118 have improper antecedent basis problems in reciting "An assay according to claim 114". Change to --The assay according to claim 114-- for proper antecedent basis.

Claim 120-123 have improper antecedent basis problems in reciting "An assay according to claim 119". Change to --The assay according to claim 119-- for proper antecedent basis.

Claim 125-128 have improper antecedent basis problems in reciting "An assay according to claim 124". Change to --The assay according to claim 124-- for proper antecedent basis.

Claim 130-133 have improper antecedent basis problems in reciting "An assay according to claim 129". Change to --The assay according to claim 129-- for proper antecedent basis.

Claim Rejections - 35 USC § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 102-103, 114-115, 119-120, and 124-125 are rejected under 35 U.S.C. 102(b) as being anticipated by Bodor et al. (Clinical Chemistry, 1992).

Bodor et al. developed monoclonal antibodies that bind cardiac specific isoform of troponin for use in troponin immunoassays (see Abstract). The characterization and specificity of the mAbs were determined using cTnI and cTnC coated microtiter plates in order to develop cTnI specific mAb-based ELISA (see page 2205, column 1 and page 2203, column 2). Bodor et al. found that two monoclonal antibodies, 3C5.10 and 1E11.3, specifically bind (enhanced reactivity) only free cTnI, a cardiac specific isoform of troponin. Bodor et al. also found that another mAb, 5D4.1, binds cTnI only when complexed with TnC. Bodor further found that 5 other mAbs independently bind both free and complexed cTnI (see page 2207, column 2). Bodor et al. teach that dependency of 5D4.1 to the presence of TnC in binding cTnI opens up possibilities for investigating TnI-TnC interactions, e.g. differentiating free TnI from TnI complexed with TnC in tissue and serum (see page 2212, column 1).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 85-93, 104-106, 116-118, 121-123, and 126-128 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bodor et al. (Clinical Chemistry, 1992).

Bodor et al. has been discussed supra. Bodor et al. fail to teach fail to teach the comparative levels of intensity signals taught in claims 85, 87, 88, 90, 91, and 93 wherein the level of signal intensity produced by antibody binding of free and complexed cardiac specific isoforms is greater by at least a factor of 2 or 5 larger than the minimum signal resulting from said antibody binding to equal number of free and complexed troponin components which do not

comprise said cardiac specific isoforms of troponin. Bodor et al. also fail to teach correlation values taught in claims 104-106, 116-118, 121-123, and 126-128 wherein detectable signal is equal, a factor of 0.2, and a factor of 2 for equal amounts of all, free and complexed, cardiac specific isoforms of troponin.

However, such correlative values comparing signal produced as effected by amount of binding of antibodies with cardiac isoform specificity and concentrations, thereof in comparison to that of non-cardiac isoform specificities in troponin assays represent result effective variables which the prior art references have shown may be altered in order to achieve optimum results. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum of workable ranges by routine experimentation." Application of Aller, 220 F.2d 454, 456, 105 USPQ 233, 235-236 (C.C.P.A. 1955). "No invention is involved in discovering optimum ranges of a process by routine experimentation." Id. at 458, 105 USPQ at 236-237. The "discovery of an optimum values of a result effective variables in a known process is ordinarily within the skill of the art." Application of Boesch, 617 F.2d 272, 276, 205 USPQ 215, 218-219 (C.C.P.A. 1980). Since Applicant has not disclosed that the specific limitations recited in instant claims 85, 87, 88, 90, 91, 104-106, 109-111, 116-118, 121-123, and 126-128 are for any particular purpose or solve any stated problem and the prior art teaches that the level of antibody binding is a function of specificity toward a particular isoform, and results often vary according to the amount of mAbs that bind the free and/or complexed cardiac specific isoform of troponin present in the serum sample being analyzed, parameters appear equivalent to that taught

and shown by prior art. Absent unexpected results, it would have been obvious for one of ordinary skill to discover the optimum workable ranges of the teachings and methods disclosed by the prior art by normal optimization procedures known in troponin assays.

7. Claims 94-96 and 129-133 are rejected under 35 U.S.C. 103(a) as being unpatentable over Katus et al. (Clinical Chemistry, 1992) in view of Bodor et al. (Clinical Chemistry, 1992).

Katus et al. teach performing immunoassay- ELISA for cardiac Troponin T (TnT) using two monoclonal antibodies that are cardiac specific isoforms of TnT (see page 387). Katus et al. teach that TnT exists in three isoforms, one of which is cardiac specific (see page 386). Katus et al. teach that the mAbs 1B10 and M7 specifically bind cardiac specific TnT isoform. However, only mAb M7 differentially and specifically binds the cardiac specific TnT isoform. 1B10 cross-reacts with non-cardiac specific TnT isoform.

Katus et al. differ in failing to teach performing an immunoassay wherein an antibody specifically binds to both free cardiac specific TnT and complexed cardiac specific TnT.

Bodor et al. has been discussed supra.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to develop monoclonal antibodies that specifically bind cardiac specific isoforms of TnT and characterize their specificity either to free or complexed forms such as taught by Bodor in cardiac specific TnC isoform because generation and characterization of monoclonal antibodies are conventional and well-known in the art. One of ordinary skill in the art at the time

of the instant invention would have been motivated to develop such antibodies which exhibit specific dependency on the complexation of an antigen to bind because Bodor specifically taught that dependency of binding on the existence of an antigen in a complex form opens up possibilities for investigating complex interactions, i.e. TnI-TnT or TnC-TnT interactions, so as to differentiate the kinetics between free and complexed TnT in tissue and serum.

Katus et al. and Bodor et al. fail to teach the comparative levels of intensity signals taught in claims 94 and 96 wherein the level of signal intensity produced by antibody binding of free and complexed cardiac specific isoforms is greater by at least a factor of 2 or 5 larger than the minimum signal resulting from said antibody binding to equal number of free and complexed troponin components which do not comprise said cardiac specific isoforms of troponin. Katus et al. and Bodor et al. also fail to teach correlation values taught in claims 131-133 wherein detectable signal is equal, a factor of 0.2, and a factor of 2 for equal amounts of all, free and complexed, cardiac specific isoforms of troponin.

However, such correlative values comparing signal produced as effected by amount of binding of antibodies with cardiac isoform specificity and concentrations, thereof in comparison to that of non-cardiac isoform specificities in troponin assays represent result effective variables which the prior art references have shown may be altered in order to achieve optimum results. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum of workable ranges by routine experimentation." Application of Aller, 220 F.2d 454, 456, 105 USPQ 233, 235-236 (C.C.P.A. 1955). "No invention is involved in

discovering optimum ranges of a process by routine experimentation." Id. at 458, 105 USPQ at 236-237. The "discovery of an optimum values of a result effective variables in a known process is ordinarily within the skill of the art." Application of Boesch, 617 F.2d 272, 276, 205 USPQ 215, 218-219 (C.C.P.A. 1980). Since Applicant has not disclosed that the specific limitations recited in instant claims 94-96 and 131-133 are for any particular purpose or solve any stated problem and the prior art teaches that the level of antibody binding is a function of specificity toward a particular isoform, and results often vary according to the amount of mAbs that bind the free and/or complexed cardiac specific isoform of troponin present in the serum sample being analyzed, parameters appear equivalent to that taught and shown by prior art. Absent unexpected results, it would have been obvious for one of ordinary skill to discover the optimum workable ranges of the teachings and methods disclosed by the prior art by normal optimization procedures known in troponin assays.

8. For reasons aforementioned, no claims are allowed.

Information Disclosure Statement

9. The Information Disclosure Statement (PTO-1449) filed 10/1/99 in Paper No. 3 is acknowledged. References AF, AI, AJ, AM, AO, AX, BB, BF, BX, BY, and CB were not considered because a copy of the references were not provided. References AE and AH were not considered because neither an English translation nor a statement of relevancy was provided

therefor. References AU and BC (Indexes) were not considered because no relevant information can be derived therefrom nor a statement of relevancy was provided therefor.

Remarks

10. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Isawa et al. (US 5,141,736) discloses the production of polydomas by fusing a hybridoma which produces an antibody with another hybridoma which produces an antibody against another a target antigen (see column 6, lines 11-45). This fusion produces hybrid monoclonal antibodies which retain the ability to bind both target antigens (see column 7, line 55- column 8, line 29).

Wick et al. (US 5,756,682) disclose a sandwich assay employing an antibody specific for cTnI as one binding partner and TnC as the other binding partner.

Jackowski et al. (US 5,747,274) discloses simultaneous detection of at least three cardiac markers the use of different monoclonal antibodies each of which is complementary to a different marker.

Buechler et al. (US 5,480,792) disclose methods for detecting the presence or amount of target ligand using antibodies which bind to the complex of ligand receptor and target ligand.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gailene R. Gabel whose telephone number is (703) 305-0807. The

examiner can normally be reached on Monday to Friday from 7:00 AM to 4:30 PM. The examiner can also be reached on alternate Fridays at 7:00 AM to 3:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, can be reached on (703) 305-3399. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

10/1/00

Gailene R. Gabel
Patent Examiner
Art Unit 1641

LONG V. LE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600